Modulation of Longevity and Tissue Homeostasis by the Drosophila PGC-1 Homolog.

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Public Summary:
In mammals, the PGC-1 proteins are key regulators of how cells generate and utilize energy. Specifically, PGC-1 proteins can regulate the number and activity of cellular structures called mitochondria, which play a fundamental role in regulating cellular energy stores. Interestingly, defects in mitochondria have been implicated in numerous diseases, including neurodegeneration and cardiomyopathy. Here, we show that overexpression of Drosophila PGC-1 (dPGC-1/spargel) is sufficient to increase mitochondrial activity, indicating it acts similarly to the mammalian proteins. Surprisingly, tissue-specific overexpression of dPGC-1 in stem and progenitor cells within the digestive tract extends life span. Long-lived flies overexpressing dPGC-1 display a delay in the onset of aging-related changes in the intestine, leading to improved tissue homeostasis in old flies. Together, these results demonstrate that dPGC-1 can slow aging both at the level of cellular changes in an individual tissue and also at the organismal level by extending life span. Our findings point to the possibility that alterations in PGC-1 activity in high-turnover tissues, such as the intestine, may be an important determinant of longevity in mammals.

Scientific Abstract:
In mammals, the PGC-1 transcriptional coactivators are key regulators of energy metabolism, including mitochondrial biogenesis and respiration, which have been implicated in numerous pathogenic conditions, including neurodegeneration and cardiomyopathy. Here, we show that overexpression of the Drosophila PGC-1 homolog (dPGC-1/spargel) is sufficient to increase mitochondrial activity. Moreover, tissue-specific overexpression of dPGC-1 in stem and progenitor cells within the digestive tract extends life span. Long-lived flies overexpressing dPGC-1 display a delay in the onset of aging-related changes in the intestine, leading to improved tissue homeostasis in old flies. Together, these results demonstrate that dPGC-1 can slow aging both at the level of cellular changes in an individual tissue and also at the organismal level by extending life span. Our findings point to the possibility that alterations in PGC-1 activity in high-turnover tissues, such as the intestine, may be an important determinant of longevity in mammals.